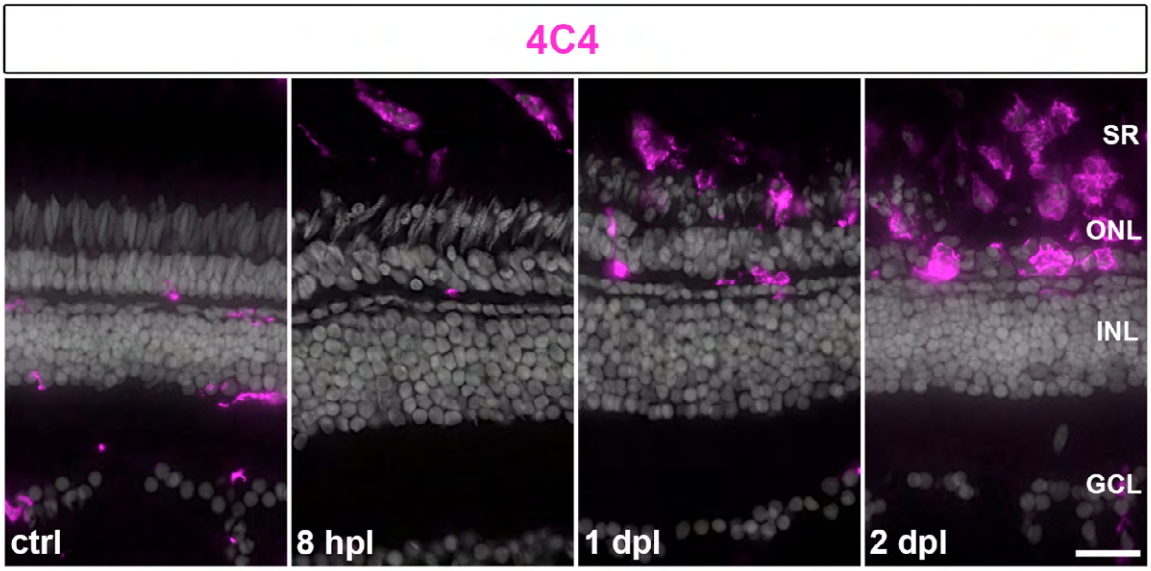
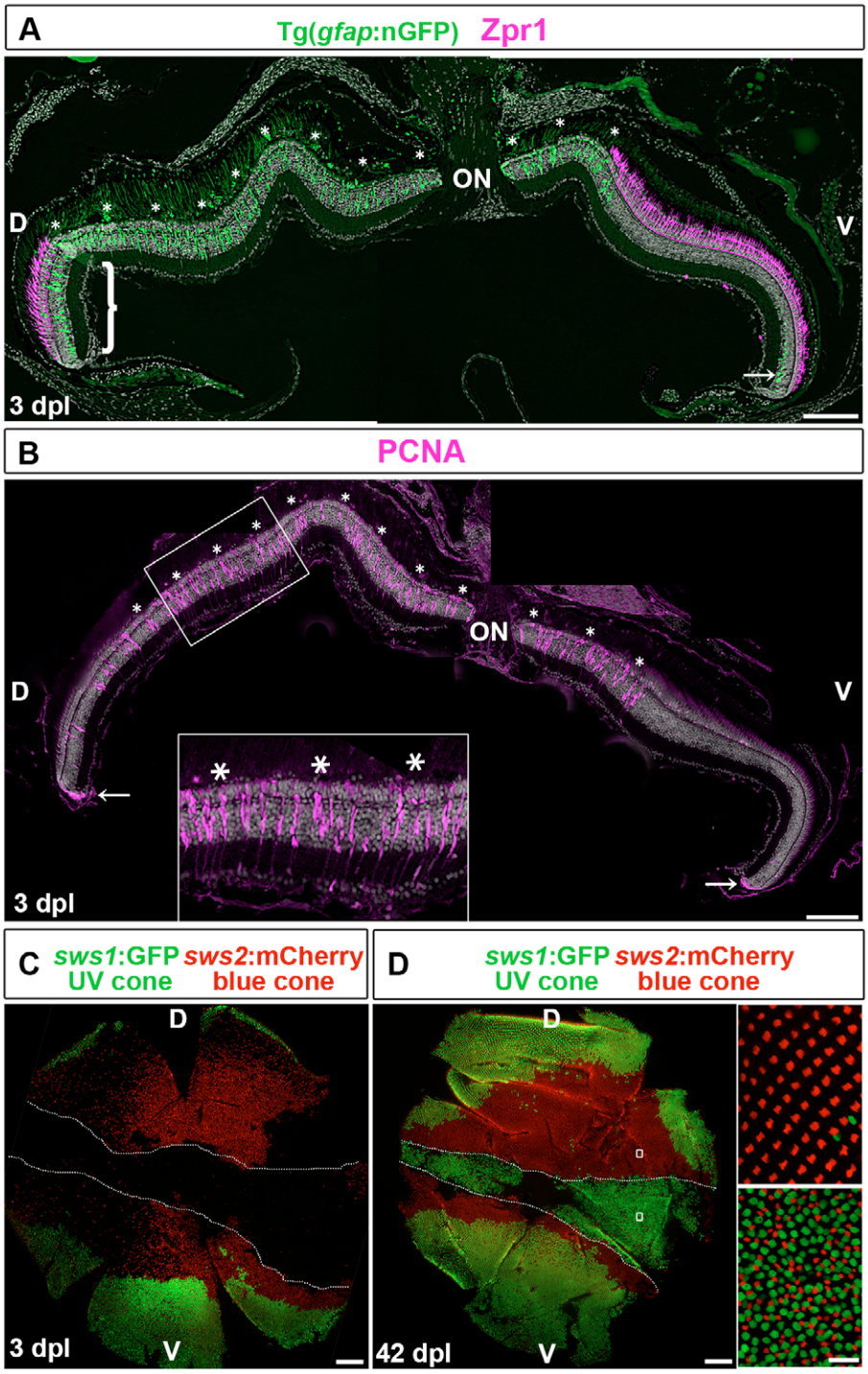
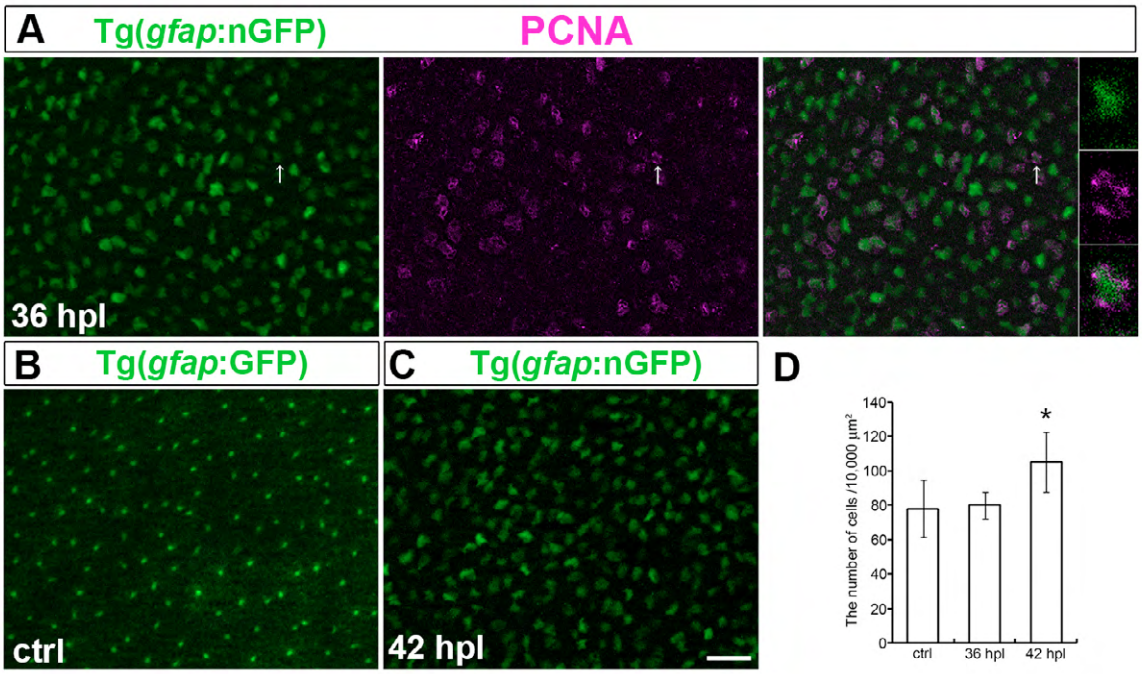


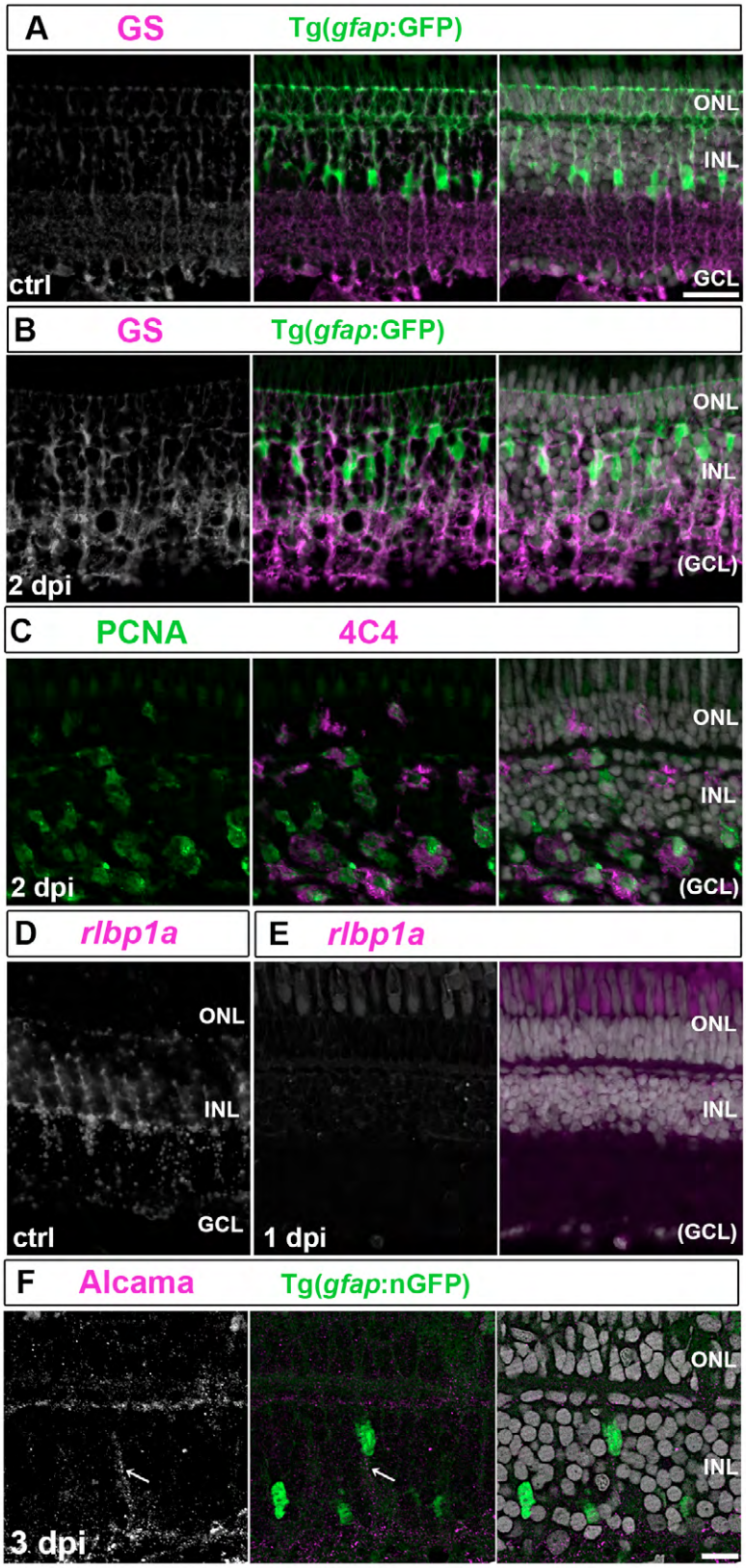
Supplementary Figure 1 (related to Figure 2) Activation of microglia at early stages after light lesion.
In the unlesioned retina, resident microglia labeled with the specific marker 4C4
(magenta) are at the boundaries of the INL and the GCL. At 8 hpl activated microglia migrate into the ONL and infiltrate through the subretinal space (SR) from the choroid circulation; they actively phagocytose photoreceptor debris at 1 to 2 dpl.
Scale: 20 μm.



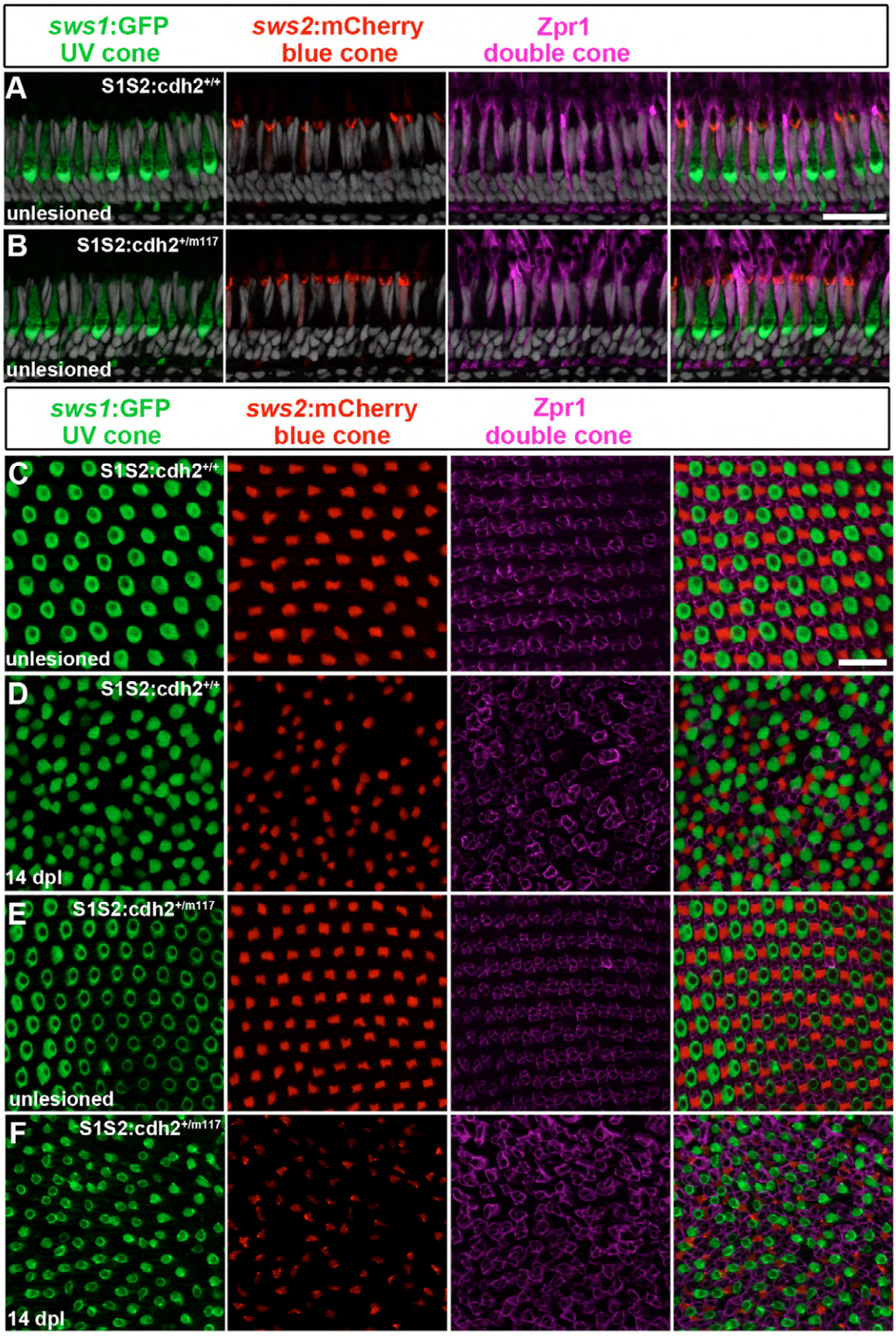
Supplementary Figure 2 (related to Figure 3) Müller glia partially dedifferentiate but fail to reenter the cell cycle when photoreceptor degeneration is confined to loss of UV cones.
(A) Immunochemistry with double cone marker, zpr1 (magenta) in retinal cryosection of light-lesioned *mi2004* fish with inducible nGFP (green) at 3 dpl; ON, optic nerve. Müller glia in dorsal (D) peripheral retina, where zpr1+ double cones are not destroyed by the intense light (bracket), re-express the nGFP reporter. Immature Müller glia at the ventral (V) margin adjacent to the CMZ express nGFP (arrow). (B) Immunocytochemistry for PCNA (magenta) in a retinal cryosection. PCNA+ neurogenic clusters at 3 dpl in the central retina where all cone subtypes are destroyed (asterisks). Inset, higher magnification of the boxed region. Progenitors in the CMZ are PCNA+ (arrows). (C) Whole, flat-mounted retina of light-lesioned (3 dpl) *Tg(sws1:GFP;sws2:mCherry)* fish. Blue (red) and UV cones (green) and red-green double cones (not shown) are missing in the central lesioned region bounded by dotted lines. UV cones (green) are ablated from most of the retina, including dorsal. (D) By 42 dpl both UV cones (green) and blue cones (red) have regenerated within the central region (dotted line). UV cones fail to regenerate in the regions where blue cones (along with red/green double cones, not shown) were spared: Boxed area dorsal to the lesion shown at higher magnification in the upper right, shows organized rows of surviving blue cones (red), but very few UV cones (green). Regenerated cones in central retina are identifiable because they fail to recreate the precisely organized cone mosaic pattern (boxed area in lower right; also see Supplementary Figure S5). Scales: 100 μm, A, B; 200 μm C, D; 20 μm, D (high magnification).



Supplementary Figure 3 (related to Figure 4) Injury-induced Müller glia reenter the cell cycle and complete cell division between 36 and 42 hpl.
(A) PCNA (magenta) immunocytochemistry on flat-mounted retina from a light lesioned *mi2004* fish with inducible nGPF (green) at 36 hpl; some nGFP+ Müller glia express PCNA (arrow). (B) Flat-mounted, unlesioned retina from *mi2002* fish with *gfap:GFP* reporter, focused at the level of the basal processes of Müller glia (green) in the inner plexiform layer. (C) Müller glia in a light-lesioned *mi2004* fish with inducible nGFP (green) in at 42 hpl. (D) Planimetric density of GFP+ Müller glial cells. Scales: 20 µm A, B, C. * $p < 0.005$.

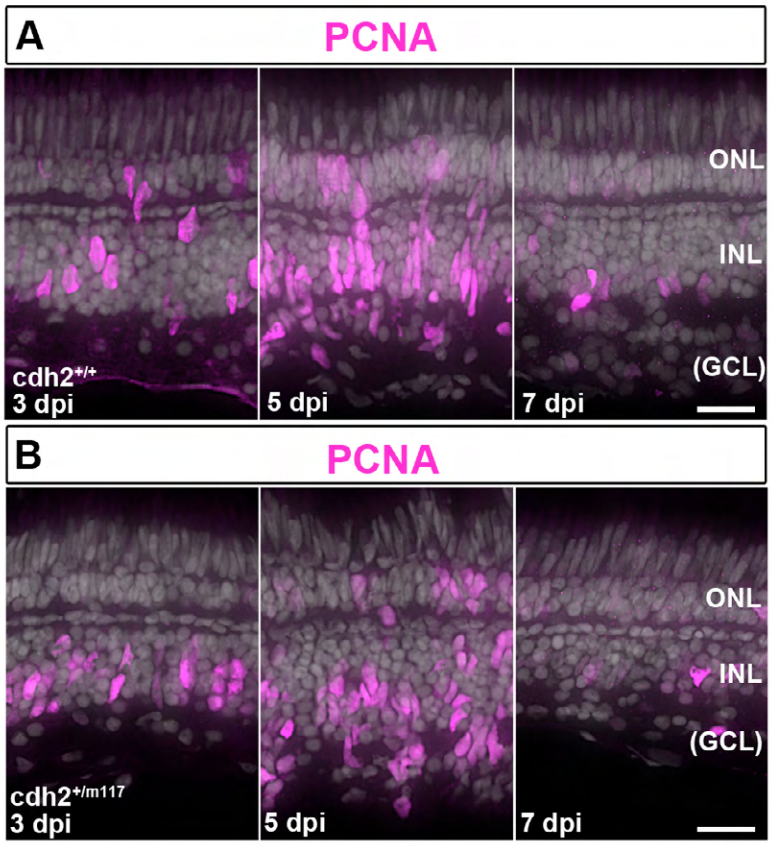


Supplementary Figure 4 (related to Figure 5) Basal processes of Müller glia collapse and markers of differentiation are down-regulated after intraocular ouabain injection.
(A, B) Immunocytochemistry for the Müller glial marker glutamine synthetase (GS) (white/magenta) in unlesioned (A) and 2 dpi (B) *gfap:GFP* retinas with Müller glial reporter (green). GS+/GFP+ Müller glial processes in the inner retina are disrupted, whereas the organization of the outer retina, including the adherens junctions at the outer limiting membrane, remain intact at 2 dpi. (C) PCNA+ (green) activated microglia (4C4+, magenta) are abundant in the damaged inner retina at 2 dpi. (D, E) *In situ* hybridization for another Müller glia marker, *rlbp1a* (white/magenta, D), shows expression is gone at 1 dpi (E). (F) Weak Alcama immunoreactivity (magenta/white) appears in the basal process (arrow) of a Müller glia with the inducible nGFP reporter (green) at 3 dpi. Scales: 20 μm, A-E; 10 μm, F.



Supplementary Figure 5 (related to Figure 6) Regeneration of cone photoreceptors in *Tg(sws1:GFP;sws2:mCherry); cdh2*$^{+/m117}$ heterozygote retinas.

(A, B) Immunocytochemistry for red/green double cone marker, zpr1 (magenta); UV cones (green), blue cones (red). In unlesioned retinas, all cone subtypes are present and appear morphologically normal in the *cdh2*$^{+/m117}$ het retinas (B) similar to the wild-type sibs (A). (C-F) Immunocytochemistry for zpr1 (magenta) in unlesioned, flat-mounted retinas illustrates the organized cone mosaic pattern in wild-type sib (C) and *cdh2*$^{+/m117}$ het retinas (E). At 14 dpl, all cone subtypes regenerate, but the mosaic pattern is not restored in sib (D) or *cdh2*$^{+/m117}$ (F). Scales: 20 μm, A-F.



Supplementary Figure 6 (related to Figure 7) Injury-induced Müller glia produce proliferating retinal progenitors, but in *cdh2*$^{+/m117}$ heterozygotes their morphology is abnormal after destruction of inner retinal neurons.
(A,B) Immunocytochemistry for PCNA (magenta) in wild-type sib and *cdh2*$^{+/m117}$ het retinas after intraocular injection of ouabain. (A) In the wild-type sib, PCNA is expressed in Müller glial nuclei that migrate apically at 3 dpi, and PCNA+ progenitors form elongated, spindle-shaped neurogenic clusters at 5 dpi. The number of PCNA+ cells decreases at 7 dpi. (B) In the *cdh2*$^{+/m117}$ hets, at 5 dpi PCNA+ progenitors fail to form cohesive, neurogenic clusters, and their nuclei are rounded, rather than spindle-shaped. The number of PCNA+ cells is reduced at 7 dpi, as in wild-type sibs. Scales: 20 μm, A,B.

Table S1. Antibody list

name	antibody description	Manufacturer	concentration
PCNA	rabbit polyclonal	Abcam	1:400
PCNA	mouse monoclonal	Sigma	1:1000
Rx1	guinea pig polyclonal	Open Biosystems	1:200
BLBP	rabbit polyclonal	Abcam	1:1000
zn5	mouse monoclonal	Zebrafish International Resource Center	1:500
pH3	rabbit polyclonal	UPState	1:1000
BrdU	rat monoclonal	Accurate chemical	1:50
BrdU	mouse monoclonal	Invitrogen	1:100
HuC/D	mouse monoclonal	Molecular Probes	1:1000
N-cadherin	rabbit polyclonal	Liu et al. 2001	1:500
GS	mouse monoclonal	CHEMICON	1:100
4C4	mouse monoclonal	Jonathan Scholes, University College London	1:200
zpr1	mouse monoclonal	Zebrafish International Resource Center	1:200
GFP	rabbit polyclonal	Invitrogen	1:500